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10/642,763	08/19/2003	Francisco Veas	GRT/1721-67	3291

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EXAMINER

HUMPHREY, LOUISE WANG ZHIYING

ART UNIT	PAPER NUMBER
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1648

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12/28/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/642,763	Applicant(s) VEAS, FRANCISCO	
	Examiner Louise Humphrey, Ph.D.	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 October 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 22-24, 26-33, 35-38 and 40-51 is/are pending in the application.
- 4a) Of the above claim(s) 45, 46, 48 and 49 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 22-24, 26-33, 35-38, 40-44, 47, 50 and 51 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>10/10/07</u> . | 6) <input type="checkbox"/> Other: _____ |

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10 October 2007 has been entered.

DETAILED ACTION

This Office Action is in response to the amendment filed 10 October 2007 and 10 September 2007. Claims 1-21, 25, 34 and 39 have been cancelled. Claims 50 and 51 have been added. Claims 22-24, 26-33, 35-38 and 40-51 are pending. Claims 45, 46, 48 and 49 are drawn to a nonelected subject matter and hence are withdrawn from further consideration pursuant to 37 CFR 1.142(b). Claims 22-24, 26-33, 35-38, 40-44, 47, 50 and 51 are currently examined.

The objection to the specification is **maintained** because Applicant only appended SEQ ID NO. to the sequence on page 13 but not to the sequences on page 17-19.

Claim Rejections - 35 USC § 101

35 U.S.C. §101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The rejection of claims 22 and 42 under 35 U.S.C. §101, as being inoperative and therefore lacking patentable utility is **withdrawn** in view of the scope of enablement rejection.

Claim Rejections - 35 USC § 112, 1st ¶, scope of enablement

The following is a quotation of the first paragraph of 35 U.S.C. §112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 22 and 42 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification commensurate in scope is **maintained and extended to claims 23, 24, 26-28, and 50.**

Claims 22-24, 26-28, 42 and 50 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for an immunogenic composition comprising a complex formed by incubating a first cell expressing CD4/CCR5/CXCR4 and a second cell expressing HIV gp120 and/or gp41 in contact with a fixing agent, aldidrithiol-2 or formaldehyde, does not reasonably provide enablement for any other two-cell complex between any other pathogenic target and any other receptor in contact with any other binding agent. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors

(MPEP §2164.01(a)). See, *In re Wands*, 8 USPQ2d 1400, at 1404 (CAFC 1988); and *Ex Parte Forman*, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Id.* While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered.

The instant claims are drawn to an immunogenic composition comprising a two-cell complex formed by interaction between a receptor-binding region and a receptor from a pathogenic agent, being expressed on the first and second cells, respectively. The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:

The disclosure fails to provide sufficient guidance pertaining to the structural characteristics of the pairs of target and receptors that are capable of interacting and undergoing conformational changes to form fusion intermediates in a specific time frame and hypothetically exposing the fusion intermediate epitopes that elicit an antibody or serum. The disclosure also fails to provide any guidance pertaining to the molecular determinants of those regions of the infectious pathogenic agent and cell surface receptors that are involved in fusion, which might enable the skilled artisan rationally direct molecules toward certain active sites in the fusion reaction. However, without sufficient guidance pertaining to a suitable molecular target, the skilled artisan

has only been extended an undue invitation to further experimentation to ascertain which molecules might function in the desired manner.

The claims do not provide any structural limitations on the binding agent. Thus, any chemical compound, including *inter alia*, organic compounds, peptide mimetics, and antibodies, may be encompassed by the claims. However, the specification fails to guide the skilled artisan toward those compounds that can reasonably be expected to retain the desired "binding" activity.

The disclosure fails to provide sufficient working embodiments that support the full scope of the claimed invention. The working examples only provide method steps of making the two-cell complex of an HIV fusion intermediate. Therefore, the amount of direction is limited to how to arrest the two cells expressing CD4-CCR5/CXCR4 and gp120/gp41, respectively, at different stages of a fusion event using Aldrithiol-2 (AT-2), an oxidizing agent that inactivate HIV by disruption of nucleocapsid protein (p7) zinc finger motifs.

The prior art is unpredictable and fails to provide sufficient illumination pertaining to the structural constraints governing pathogen-cell fusion. The general state of the art only teaches arresting HIV-cell fusion intermediates. The art does not teach capturing different stages of fusion between a host cell and other infectious pathogenic agent like a non-enveloped virus or bacterium. However, no such guidance is available for the claimed target of interest and receptor in the specification. The disclosure fails to provide sufficient working embodiments to enable the full breadth of the claimed invention.

Claims 41 and 51 are drawn an isolated serum or antibody against the two-cell complex. The breadth of the claims encompasses two types of antibody: neutralizing and non-neutralizing antibody. While being enabling for non-neutralizing antibody, the specification does not reasonably provide enablement for any neutralizing antibody. The specification only states the desired goal of injecting the two-cell fusion-intermediate complexes into mammals. However, the specification is absent any specific guidance to the generation of any type of antibody or sera. The disclosure fails to provide any working embodiments that meet the claimed limitations. The working examples only provide method steps of making the two-cell fusion intermediate complex. At the time the invention was made, successful generation of neutralizing antibody or serum against such fusion intermediates was difficult and highly unpredictable to those skilled in the art (Nunberg, 2002; Lee, 1997). The Nunberg reference cited by Applicant in the response filed on 10 October 2007 reported a specific cytotoxic effect of the sera against these cell complexes. This unappreciated cytotoxicity significantly reduces both the potency and the breadth of primary virus neutralization. Lee *et al.* (1997) cautioned that a monoclonal antibody (MAb) which can block in a coreceptor binding assay may not have a neutralizing activity and, as already described for CG10 MAb, may have an augmenting activity in the fusion and infectivity assays. Studies show that access to the CD4-induced coreceptor-binding domain on gp120 is largely blocked at the fusing cell interface and is unlikely to represent a target for neutralizing antibodies (Finnegan *et al.*, 2001). These evidences clearly show the

difficulty and unpredictability in eliciting neutralizing antibody or sera against fusion-intermediate two-cell complexes.

Legal precedence dictates that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification. *In re Fisher*, 427 F.2d 833, 839, 166 U.S.P.Q. 18 24 (C.C.P.A. 1970). *In re Vaeck*, 20 U.S.P.Q.2d 1438 (C.A.F.C 1991). *In re Angstadt*, 537 F.2d 498, 502-03, 190 U.S.P.Q. 214, 21 (C.C.P.A. 1976). Thus, when all the aforementioned factors are considered *in toto*, it would clearly require undue experimentation from the skilled artisan to practice the claimed invention.

Claim Rejections - 35 USC § 112, 1st ¶, written description

The following is a quotation of the first paragraph of 35 U.S.C. §112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 22-24, 26-28, 41, 42, and 50 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The factors considered in the Written Description requirement are (1) *level of skill and knowledge in the art*, (2) *partial structure*, (3) *physical and/or chemical properties*,

(4) *functional characteristics alone or coupled with a known or disclosed correlation between structure and function*, and the (5) *method of making the claimed invention*.

Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient."

M.P.E.P. §2163.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, at the time the invention was made, of the specific subject matter claimed. The courts have stated:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); *In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in

possession of the claimed genus. (See Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, especially page 1106 3rd column). A "representative number of species" means that the species that are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. MPEP §2163 II.A.3a.ii.

Although the M.P.E.P. does not define what constitutes a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad genus. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

Vas-Cath Inc. v. Mahurkar ((CAFC, 1991) 19 USPQ2d 1111) clearly states that "Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See *Vas-Cath* at page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC §112 is severable from its enablement provision (see *Vas-Cath* at page 1115).

In the instant case, the claims are directed to an immunogenic composition comprising a two-cell complex formed by interaction between a receptor-binding region

and a receptor from a pathogenic agent, being expressed on the first and second cells, respectively, and further comprising an inert vehicle acceptable for administration to a mammal. The claim limitations, "binding agent," "target receptor(s)" and "regions of the infectious pathogenic agent recognizing the target receptor(s)," encompass an inordinate number of species that are neither described nor contemplated by Applicants. The genus of "target receptors" encompasses all bacterial adhesin receptors such as maltose-binding protein (MBP) receptor, dextran receptor, lectin receptor, integrins, amylose-binding protein (ABP) receptor (Jenkinson *et al.*, 1997) and cell surface receptors like heparin sulfate proteoglycans and CD4 and coreceptors such as CXCR4 and CCR5, while the genus of "receptor-binding region from a pathogenic agent" encompasses a wide variety of molecules including fibronectin, MBP, ABP, lectin, dextran, (Jenkinson *et al.*, 1997), and glycoproteins of all enveloped viruses (Hughson, 1997). The specification lacks sufficient variety of species to reflect this variance in the three genera. These limitations not adequately described because the specification only provides description for one or two species for each genus. The specification identifies said "target receptors" as only HIV CCR5-CD4 and said "regions of the infectious pathogenic agent" as HIV gp120 or gp120-gp41. Moreover, the specification never mentions the "binding agent" while it describes the significance of a fixing agent, aldidrithiol-2 (AT-2) or formol, for stopping fusion without significantly denaturing the epitopes of interest (page 8). Although two species of the binding agent are disclosed, the AT-2 and formol do not represent the large number of chemical compounds that fall

within the scope of "binding agent." Therefore, Applicants have not conveyed possession of the invention with reasonable clarity to one skilled in the art.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 22, 26, 29, 30, 36 and 37 under 35 U.S.C. §102(a) as being anticipated by Schønning *et al.* (02 August 1999) is **withdrawn** in response to Applicant's submission of the English translation of the French patent 99 01 794. The priority filing date has been accorded.

The rejection of claims 22, 31, 38-39 and 41 under 35 U.S.C. §102(b) as being anticipated by DeVico *et al.* (1995) is **withdrawn** in response to Applicant's amendment narrowing the scope from "means" to "cells" in the claimed invention.

The rejection of claims 22, 31, 38-39 and 41 under 35 U.S.C. §102(b) as being anticipated by Kwong *et al.* (1998) is **withdrawn** in response to Applicant's amendment narrowing the scope from "means" to "cells" in the claimed invention.

The rejection of claims 22-24, 26-33, 35-37, 41 and 44 under 35 U.S.C. §102(b) as being anticipated by La Casse *et al.* (15 January 1999) is **maintained and extended**

to claims 42, 50 and 51. Applicant's arguments have been fully considered but are not persuasive.

The instant claims are drawn to an immunogenic composition comprising a two-cell complex formed by interaction between a receptor-binding region and a receptor from a pathogenic agent, being expressed on the first and second cells, respectively, and further comprising an inert vehicle acceptable for administration to a mammal.

The instant claims are product-by-process claims and are not limited to the manipulations of the recited steps, only the structure implied by the steps. See MPEP § 2113:

"[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted).

La Casse *et al.* teach a co-culture of COS-7 cells transfected with plasmid vectors encoding HIV envelope protein gp120 and a second cell type transfected with plasmid vectors encoding the receptor U87-CD4-CCR5, which allows for cell-cell fusion. The cell complexes were fixed with 0.2% formaldehyde in phosphate-buffered saline (PBS) for immunization in mice. See page 361, 3rd column, Notes No. 9-12. PBS is an

inert vehicle that can be administered to mammals. Sera were isolated from immunized mice. See page 359, 3rd column, line 7-19.

Applicant argues that the La Casse teaching was not enabling because the cited reference's conclusion that serum raised against their immunogen contains neutralizing antibodies was subsequently retracted by the senior author (Nunberg, 2002). However, the retraction was about the neutralizing antibodies, which is not a claim limitation. Applicants are reminded that the claims are only directed toward an immunogenic composition comprising a two-cell complex formed by interaction between a receptor-binding region, being expressed on a first cell, and a receptor from a pathogenic agent, being expressed on a second cell. Applicants' arguments directed toward the ability of the two-cell complex to induce neutralizing antibodies are not relevant because they are not claimed. In summary, Applicants argued that the cited prior art, La Casse *et al.* do not teach neutralizing antibodies. However, neutralizing antibodies is not germane to the patentability of the invention claimed in the instant application. Therefore, the prior art clearly teaches the claimed immunogenic composition comprising the two-cell complex.

Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993) (Claims to a superconducting magnet which generates a "uniform magnetic field" were not limited to the degree of magnetic field uniformity required for Nuclear Magnetic Resonance (NMR) imaging. Although the specification

disclosed that the claimed magnet may be used in an NMR apparatus, the claims were not so limited.); *Constant v. Advanced Micro-Devices, Inc.*, 848 F.2d 1560, 1571-72, 7 USPQ2d 1057, 1064-1065 (Fed. Cir.), cert. denied, 488 U.S. 892 (1988) (Various limitations on which appellant relied were not stated in the claims; the specification did not provide evidence indicating these limitations must be read into the claims to give meaning to the disputed terms.); *Ex parte McCullough*, 7 USPQ2d 1889, 1891 (Bd. Pat. App. & Inter. 1987) (Claimed electrode was rejected as obvious despite assertions that electrode functions differently than would be expected when used in nonaqueous battery since "although the demonstrated results may be germane to the patentability of a battery containing appellant's electrode, they are not germane to the patentability of the invention claimed on appeal."). See MPEP §2145 (VI).

NEW Claim Rejections - 35 USC § 102

Claims 41 and 51 are directed to an isolated serum or antibody formed against the composition obtained by interaction of a receptor-expressing cell and a target-expressing cell in contact with a binding agent. There are no claim limitations on the binding epitopes, so the instant claims read on any antibody including an anti-CD\$-gp120 antibody, anti-CD4 antibody, anti-CCR5 antibody, anti-CXCR4 antibody, anti-gp120 antibody, anti-gp41 antibody, or anti-gp120/gp41 antibody.

Claims 41 and 51 are rejected under 35 U.S.C. §102(b) as being anticipated by Thali *et al.* (1993).

Thali *et al.* teach antibodies 17b and 48d that targets a CD4-induced epitope on the gp120-CD4 complex but also binds isolated gp120. See page 3980. Thus, the instant invention is anticipated by Thali *et al.*

Claims 41 and 51 are rejected under 35 U.S.C. §102(b) as being anticipated by Lee *et al.* (1997).

Lee *et al.* teach a gp120-CD4-specific monoclonal antibody CG10. See page 6037, 2nd column, line 5-8. Thus, the instant invention is anticipated by Lee *et al.*

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The rejection of claims 22, 25 and 41 under 35 U.S.C. §103(a) as being obvious over DeVico *et al.* (1995) or Kwong *et al.* (1998) in view of Rigaud *et al.* (1994) is **withdrawn** in response to Applicants' amendment.

Applicant argued against all the other rejections based on the same reason as set forth above for the primary reference, La Casse *et al.*, that the reference was not enabled because the results of neutralizing antibodies were retracted.

The rejection of claims 22 and 40 under 35 U.S.C. §103(a) as being obvious over La Casse *et al.* (1999) in view of Rossio *et al.* (1994) is **maintained** for the same reason as indicated above.

The rejection of claims 22-24, 26-33, 35-38, 40 and 41 under 35 U.S.C. §103(a) as being obvious over La Casse *et al.* (1999) in view of Riley *et al.* (1998) is **maintained** for the same reason as indicated above.

The rejection of claims 24, 43, 44 and 47 under 35 U.S.C. §103(a) as being obvious over La Casse *et al.* (1999) in view of Murphy *et al.* (1990) is **maintained** for the same reason as indicated above.

Correspondence

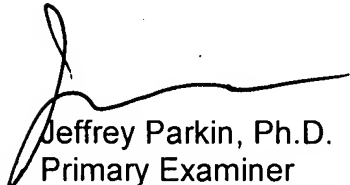
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey, Ph.D. whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9:30 am - 5:30 pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached at 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



Jeffrey Parkin, Ph.D.
Primary Examiner
12 December 2007



Louise Humphrey, Ph.D.
Assistant Examiner